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EXAMINER

LY, CHEYNE D

ART UNIT PAPER NUMBER

1631

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/088,245

Applicant(s)

ANTSON ET AL.

Examiner

Cheyne D Ly

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 and 34-41 is/are pending in the application.
- 4a) Of the above claim(s) 10-26, 29-32, and 34-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 27 and 28 is/are rejected.
- 7) ☒ Claim(s) 27 and 28 is/are objected to.
- 8) ☒ Claim(s) 1-32 and 34-41 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 07/03/02.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traversal of Group I, claims "11-9, 27 and 28", filed March 15, 2004, is acknowledged.
2. The traversal is on the ground(s) that it would not be unduly burdensome to perform a search on Groups I-III together due to said groups being classified "in the same class 702, subclass 270." This is not found persuasive because the classification of the respective groups in the same class and subclass does not change the fact the distinct groups are directed to either a specific composition or distinct methods. Each group has distinct critical limitations which necessitate an undue search burden if they were search together.
3. The requirement is still deemed proper and is therefore made FINAL.
4. Further, Applicant cites groups I-III being classified "in the same class 702, subclass 270" which is incorrect. Groups I-III have been classified in class 702, subclass 27, as recited in the Written Restriction Requirement, mailed January 29, 2004.
5. Further, it is noted that Applicant has inadvertently elected "Group I, claims 11-9, 27 and 28" to begin prosecution of the instant application. In order to advance prosecution, it has been assumed that the recitation of "claims 11-9" in Applicant's response to the Restriction Requirement is a typographical error. Therefore, claims 1-9, 27, and 28, directed to Group I, are examined on the merits.
6. Claims 1-9, 27, and 28 are examined on the merits.

ABSTRACT

7. It is noted that Applicant has submitted the first page of a PCT published application to be used an abstract for this instant Application. It is suggested that Applicant submit an abstract

Art Unit: 1631

commencing on a separate sheet of paper to avoid any future complications in the event that the instant Application is issued as a patent. It is further noted that this is not a requirement but a suggestion to avoid future complications that would impede the instant Application from being issued.

DRAWING

8. The disclosure is objected to because of the following informalities: The figures contain capital letter designation (for example, Fig. 1A) for the respective figures while the Brief Description of the Drawings contain lower letter designations (for example, Figure 1a). Appropriate correction is required to resolve the inconsistency.

SEQUENCE COMPLIANCE

9. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). See, for example, Figure 1B. However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because Figure 1B, contains amino acid sequences with sequence lengths that are equal to or greater than 4 amino acid molecules and these sequences do not have SEQ ID Nos cited along with each sequence in the specification or Figure. Applicants are also reminded that SEQ ID Nos are not required in Figures per se, however, the corresponding SEQ ID Nos then are required in the Brief Description of the Drawings section in the specification. Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicant(s) are required to submit a computer readable form sequence listing, a paper copy for the specification, and statements under 37 CFR § 1.821(f) and (g). Applicant(s) are given the same response time regarding this

Art Unit: 1631

failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

OBJECTIONS

10. The title of the invention is not descriptive because the instant title is directed to “Target for...therapy” while the claimed invention is directed to a crystal composition. A new title is required that is clearly indicative of the invention to which the claims are directed.

11. Claim 27, line 4, is objected to because of the following informalities: Line 3 is missing a comma and a space between “3” and “or”. Appropriate correction is required.

12. Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 27 defines specific amino acids of E2NT according to Table 3. Claim 28, which depends from claim 27, recites the molecule or molecular complex without reciting any specific amino acids defined by Table 3. Therefore, the broad limitations of claim 28 do not further limit claim 27 from which claim 28 depend. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

13. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (Page 63, Line 1). Applicant(s) is/are required to delete the embedded hyperlink and/or other form of browser-executable code, or inactivate the hyperlink.

See MPEP § 608.01.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-9, 27, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

16. Specific to claim 1, line 1, and claim 8, line 2, Applicant uses the abbreviations of "E2". Abbreviations in claims are vague and indefinite unless accompanied by the full name, usually in parentheses. Claims 2-9 are rejected for being dependent from claim 1.

17. Specific to claim 1, line 2; claim 27, line 4; and claim 28, line 3, the phrase "homologue thereof" causes said claim to be vague and indefinite because it is unclear what criteria is being used to determine a homologue. Are homologues determined by sequence similarity, structure similarity, or other classification parameters. Clarification of the metes and bounds is required. Claims 2-9 are rejected for being dependent from claim 1.

18. Specific to claim 3, line 3; claim 5, line 2; claim 6, line 2; and claim 7, line 2, the Applicant uses the abbreviations of "N1" or "N2". Abbreviations in claims are vague and indefinite unless accompanied by the full name, usually in parentheses. Claim 4 is rejected for being dependent from claim 3.

CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

Art Unit: 1631

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF WRITTEN DESCRIPTION

20. Claims 1-9, 27, and 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

21. The specification discloses the crystal of E2NT protein and its corresponding atomic coordinates (page 28-66) and protein sequence (Fig. 1.B). However, claims 1-9, 27, and 28 are directed to encompass homologue or homologue thereof of the E2NT protein. None of these homologues meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

22. With the exception of crystal of E2NT protein and its corresponding atomic coordinates (page 28-66) and protein sequence (Fig. 1.B), the skilled artisan cannot envision the detailed chemical structure of the encompassed the homologous crystal and/or proteins of the claimed, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and

Art Unit: 1631

Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:
...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention."
Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

23. Therefore, only crystal of E2NT protein and its corresponding atomic coordinates (page 28-66) and protein sequence (Fig. 1.B), but not the full breadth of the claims 1-9, 27, and 28 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

LACK OF ENABLEMENT IN SCOPE

24. Claims 1-9, 27, and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal structure of the E2NT protein wherein the corresponding atomic coordinates (page 28-66) and protein sequence (Fig. 1.B) are instantly disclosed, does not reasonably provide enablement for making crystals for the "homologue thereof" of the E2NT protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Art Unit: 1631

25. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

26. It is acknowledged that Applicant has disclosed information to enable one skilled in the art to make a specific crystal of the E2NT protein wherein the corresponding atomic coordinates (page 28-66) and protein sequence (Fig. 1.B) are provided. The instant specification discloses that the crystal of the E2NT protein has been derived via a protein crystallization method (page 28-66). It is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). A method that relies on data from an unpredictable art such as protein crystallization would require clear and precise guidance for one skilled in the art to reliably use the said method. Further, as recently as November 1, 2002, Science published a New Focus article depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essence, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which results in high failure rate for proteins that are

Art Unit: 1631

being crystallized. Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (New Focus, Science, 2002). Accordingly, it would be unpredictable for one skilled in the art to make crystal structures of any protein beyond the one of the instant case as commensurate in scope with the instant claims. In light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to use the information disclosed for one specific crystal to predictably make crystal structures of “homologous thereof” of the E2NT protein without undue experimentation.

Claim Rejections - 35 USC § 102

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

28. Claims 1-5 and 7-9 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Harris et al. (June 1999).

29. It noted that the limitations of N1 and N2 have been rejected under 35 U.S.C. 112, second paragraph, as being vague and indefinite due to the abbreviations being undefined. Therefore, said limitations have been construed as broadly as reasonable in the instant prior art rejection.

30. Harris et al. discloses a crystal structure of E2 N-terminal module (E2NT) protein which regulates viral transcription and DNA replication (Abstract etc. and page 1673, column 3, lines 5-22, and Table 1), as in instant claim 8.

31. “The E2 DBD dimerizes to form a β barrel in the DNA binding site” (page 1673, column 1, lines 19-22), as in instant claim 1.

Art Unit: 1631

32. The N-terminal activation core domain comprises amino acids 1 through 200 (page 1673, column 1, lines 14-19) wherein amino acids 1 and 200 lie on the opposite sides of said N-terminal, as in instant claim 2.

33. The crystal structure of Harris et al. comprises a plurality of clusters as represented by A-H (at least three clusters) in Figures 1 and 2. The hinge region that joins (interface) the AD to the DBD extends from the COOH-terminus (Figure 1 (A)), as in instant claims 3 and 4.

34. The first cluster comprises Trp92 (page 1674, column 3, line 5), as in instant claim 5.

35. The third cluster of residues comprises Pro106 (page 1676, column 1, lines 18-23), as in instant claim 7.

36. The crystal of Harris et al. comprises Glu39 (page 1674, column 1, line 25), as in instant claim 9.

CONCLUSION

37. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

38. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

Art Unit: 1631

39. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

40. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly
6/7/04

Ardin H. Marschel 6/11/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER